Correspondence

Letter by Pohjoismäki Regarding Article, “Impaired Mitochondrial Biogenesis Precedes Heart Failure in Right Ventricular Hypertrophy in Congenital Heart Disease”

To the Editor:

The recent article by Karamanlidis and coworkers1 is an attempt to address the role of mitochondrial DNA (mtDNA) in mitochondrial biogenesis and its use as a marker for mitochondrial damage in heart failure. The importance of mitochondrial biogenesis and particularly mtDNA maintenance in human heart disease is intriguing. Indeed, some of the findings presented here raise relevant questions concerning the relation of mtDNA and mitochondrial function. For example, the notion that in some cases low mtDNA levels result in increased steady-state levels of mitochondrial transcripts: Why is there a need for high mtDNA copy number if lower levels can maintain equal pools of mitochondrial mRNAs?

The study also demonstrates the difficulty with interpreting data related to specialized processes solely based on scarce human samples. Although the work relies on pediatric samples, the authors did not address how to distinguish pathological processes from normal changes caused by mitochondrial biogenesis in the postnatal heart.

The heart is a postmitotic tissue, and any postnatal growth results from the hypertrophic growth of the cardiomyocytes. Also during heart growth, mitochondrial biogenesis is activated to keep pace with the increased energy demand. In humans, this includes mtDNA, causing a drastic increase in copy number in early childhood accompanied by changes in topological organization and replication mode.3,4

In their study, Karamanlidis and colleagues1 show significantly lower mtDNA levels failing heart (median age, 0.8 years) and to a lesser extent in hypertrophy patients (median age, 6.3 years) when compared with their control subjects (median age, 12 years). The observed differences in mtDNA levels can be explained by the age differences of the patient groups alone. I acknowledge the lack of published studies of postnatal mitochondrial biogenesis in healthy human heart, but I am concerned that the majority of the findings in this report relate to the differences between infants, adolescents, and teenagers rather than actual pathology.

Before any clinical conclusions can be made, we must understand how mtDNA copy number is controlled in healthy tissue and what significance it has for the mitochondrial function. Moreover, there is certainly a demand for basic descriptive studies on postnatal mitochondrial biogenesis in human heart.

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Disclosures

None.

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References

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